REMARKS/ARGUMENTS

The Official Action dated April 22, 2003 has been carefully considered. It is believed that the amended claims and the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

35 USC §112

The Examiner has objected to claims 23-39 under 35 USC §112, first paragraph as lacking enablement. As discussed during the telephone interview, Applicants were having difficulty understanding the objection as the Examiner confirm that the specification was "enabling for a method comprising steps for increasing the serum half-life of an immune globulin such as: making an immune globulin preparation with the recited components i.e., non-ionic surface active agents in a formulation to prolong the half-life of the immune globulin; and administering parenterally the preparation to an animal in need thereof an immune globulin preparation, ...". We submit that the claims as currently of record do recite the enabled method. However, based on the telephone interview, it appeared that the Examiner did not think the use of "two or more" non-ionic surface active agents was enabled. Without agreeing with the Examiner, Applicants have amended the claim in order to recite "a" non-ionic surface active agent in order to expedite prosecution. The amendment has been made without prejudice and without acquiescing to the Examiner's objection. Applicants reserve the right to pursue any of the deleted subject matter in a further divisional, continuation or continuation-in-part application.

In the office action, the Examiner also commented that the method should include the pharmacokinetic methods to estimate the half-life of the immune globulin. As mentioned in our last response, the pharmacokinetic method is merely proof that the claimed method works. One of skill in the art would not necessarily determine the serum half-life of the immune globulin formulation each time the method was used.

In view of the foregoing, we respectfully request that the objections to claims 23-39 as lacking enablement be withdrawn.

The Examiner has objected to claims 57-73 under 35 USC §112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the Examiner states that there is no support in the specification for a "polyclonal immune globulin". We respectfully disagree with the Examiner as there is support for that term on page 15, line 24 and page 17, lines 2-3. In addition, the application describes at length the collection of the antibodies from human plasma which would result in polyclonal anti-serum.

In view of the foregoing, we respectfully request that the objections to claims 57-73 as lacking written description be withdrawn.

35 USC §102

The Examiner has rejected claims 23, 26, 31-34 and 36-37 under 35 USC §102(b) as being anticipated by Alberici et al. (WO 94/16728). We respectfully disagree with the Examiner for the reasons that follow.

The Examiner states that Alberici et al. teach a composition comprising 0.1 to 10 g of monoclonal antibodies which would fall within the claimed range of 2-10 weight %. Weight % is calculated as the number of grams per 100 ml of solution. While Alberici et al. does disclose 0.1-10 g of monoclonal antibody, it states that such an amount would be present in a solution of 1 liter (see the English language abstract of the Alberici publication). Consequently, an amount of 0.1 g to 10 g of antibody in one liter would translate to 0.01-1% by weight as we mentioned in our last response.

In view of the foregoing, we respectfully request that the objections to the claims as being anticipated by Alberici et al. be withdrawn.

35 USC §103

The Examiner has rejected claims 23-34 and 36-38 under 35 USC §103(a) as being unpatentable over Friesen (CA 1,168,152) in view of de Burgh Bradley et al. (1,303,533). We respectfully disagree with the Examiner for the reasons that follow.

The Examiner's primary reference, Friesen, is Applicants' Canadian patent on their method of producing anti-RhD polyclonal antibodies for passive immunization of humans. Friesen does not describe adding a non-ionic surfactant to the polyclonal antibodies in order to increase the serum half-life. The deficiencies in Freisen are not remedied by de Burgh Bradley. De Burgh Bradley teaches polyoxyethylene sorbitan monooleate (Tween 80) is a component in antibody solutions used in chemical reactions to determine the Rh-typing of red blood cells. De Burgh Bradley does not provide any suggestion that Tween 80 can also be advantageous in immune globulin preparations for injection into humans.

In particular, de Burgh Bradley teaches an anti Rh(D) monoclonal antibody for the typing of red blood cells. There are three descriptions of solutions containing antibodies and Tween 80. All three solutions are diluents used in immunoassays as follows:

Page 14, lines 20 to 28 – Teaches Tween 80 may be used as a component in a diluent for blending antibodies. Page 14, lines 11 to 19 describe dilutions are required for certain assays involving RhD antibodies.
Page 19, lines 28 to 34 – Teaches Tween 80 in a diluent for a solution containing peroxidase-conjugated goat anti-human IgG (no RhD antibodies) and TMB (3,3', 5,5'-tetramethyl benzidine) that is used in an ELISA assay.
Page 29 lines 9 to 17 – Teaches Tween 80 in a diluent for a solution containing RhD antibodies together with KH_2PO_4, Na_2HPO_4 and NaN_3. This solution is used in an indirect antiglobulin (IAG) assay.

In the above three described solutions, Tween 80 is included in a diluent used to dilute the antibody prior to use in an antibody assay. This is in direct contract to Friesen who teaches concentration of immune globulines. This is also contrary to the preparation of medicines for injection into humans, where one wishes to inject the smallest volume possible.

On page 8 of the Office Action, the Examiner stated that:

> "One would have a reasonable expectation of success in modifying the immune globulin preparation since the prior art already teaches preparations comprising non-ionic surface active agents as being advantageous in immune globulin preparation."

We respectfully disagree. There is no teaching in de Burgh Bradley that Tween 80 in advantageous in immune globulin preparations. The only teaching in de Burgh Bradley is that Tween 80 is a surfactant or suspending agent (page 14, lines 26 to 28). De Burgh Bradley does not teach the reason Tween 80 is added to the solutions. Thus, the only teaching in de Burgh Bradley is that Tween 80 is required in antibody solutions that are subjected to chemical reactions in immunoassays for Rh-typing of red blood cells.

On page 7, paragraph 2 of the Office Action, the Examiner correctly points out that de Burgh Bradley (page 13, lines 16-25) teaches passive immunization with such monoclonal antibody. However, that section teaches a sterile solution of the antibody formulated in "any physiologically acceptable aqueous media, for example isotonic phosphate buffered saline or serum". Tween 80 is not described as physiologically acceptable. Furthermore, the solution that contains Tween 80 described on page 29 would be lethal if injected into a patient (it includes, KH_2PO_4, Na_2HPO_4 and NaN_3).

On page 7, paragraph 3 of the Office Action, the Examiner states that "Bradley et al teach plenty of methods of combining and administration which meet the claimed limitations." We respectfully disagree. It is not clear what the Examiner means by the term "combining". De Burgh Bradley teaches administration of the monoclonal antibody

to human patients in very general terms on pages 2, 3 and 13, and only on page 13 is there any description of a pharmaceutically acceptable carrier.

Friesen specifically addresses the issue of stability on page 6, line 21 to page 7, line 1. Specifically, Friesen teaches that lyophilized formulations are stable. There is no motivation in Friesen to seek a substance to stabilize immune globulins in serum or in the final product.

Neither Friesen nor de Burgh Bradley teach that there is a need to increase the serum half life of immune globulins, and neither reference teaches surface active agents will increase half life. Furthermore, neither reference teaches that surface-active agents can be safely injected into humans.

In summary, there is no teaching in de Burgh Bradley that the addition of polyoxyethylene sorbitan monooleate (Tween 80) is advantageous in an immune globulin preparation. The only teaching is that Tween 80 is a component in antibody solutions used in chemical reactions to determine the Rh-typing of red blood cells. The Examiner has failed to prove a connection between antibody solutions used in chemical reactions and immune globulin preparations for injection into humans. To a person skilled in the art, de Burgh Bradley does not reasonably suggest that Tween 80 increases the serum half-life of an immune globulin.

In view of the foregoing, we respectfully request that the objection to the claims under 35 USC §103(a) be withdrawn.

The Commissioner is hereby authorized to charge any deficiency in fees (including any claim fees) or credit any overpayment to our Deposit Account No. 02-2095.

In view of the foregoing, we submit that the application is in order for allowance and an early indication to that effect would be greatly appreciated. Should the Examiner like to

discuss the matter, she is kindly requested to contact Micheline Gravelle at 416-957-1682 at she convenience.

Respectfully submitted,

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